

Applicant : Masatsugu Maeda et al.  
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REMARKS

Applicants hereby submit that the enclosures fulfill the requirements under 37 C.F.R. §1.821-1.825. The amendments in the specification merely insert the paper copy of the Sequence Listing and sequence identifiers in the specification and correct certain typographical errors. No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment.

Please apply any charges or credits to Deposit Account No. 06-1050, referencing attorney docket number 06501-096001.

Respectfully submitted,

Date:

Dec 30, 2002

Janis K. Fraser

Janis K. Fraser, Ph.D., J.D.  
Reg. No. 34,819

Fish & Richardson P.C.  
225 Franklin Street  
Boston, Massachusetts 02110-2804  
Telephone: (617) 542-5070  
Facsimile: (617) 542-8906

**“Version With Markings to Show Changes Made”**

In the specification:

Paragraph beginning at page 2, line 24, has been amended as follows:

Though the sites on receptors binding with these cytoplasmic tyrosine kinases (JAK kinases) are conserved among family members, the homology is not very high (Murakami et al., Proc. Natl. Acad. Sci. USA, 88:11349-11353, 1991). Actually, the sequence that best characterizes these hemopoietin receptors exists in the extracellular region. In particular, a five amino acid motif, Trp-Ser-Xaa-Trp-Ser (SEQ ID NO:22), (wherein “Xaa” is an arbitrary amino acid), is conserved in almost all of the hemopoietin receptors. Therefore, novel receptors may be obtained by searching for novel family members using this sequence. In fact, these approaches have already led to the identification of the IL-11 receptor (Robb et al., J. Biol. Chem., 271:13754-13761, 1996), the leptin receptor (Gainsford et al., Proc. Natl. Acad. Sci. USA, 93:14564-8, 1996), and the IL-13 receptor (Hilton et al., Proc. Natl. Acad. Sci. USA, 93:497-501, 1996).

Paragraph beginning at page 3, line 10, has been amended as follows:

Initially, the inventors attempted to find a novel receptor using oligonucleotides encoding the Trp-Ser-Xaa-Trp-Ser (SEQ ID NO:22) motif[,] (WS motif), as the probe by plaque hybridization, RT-PCR method, and so on. However, it was extremely difficult to strictly select only those to which all 15 nucleotides that encode the motif would completely hybridize under the usual hybridization conditions, because the oligonucleotide tggag(t/c)nnntggag(t/c) (SEQ ID NO:21), (wherein “n” is an arbitrary nucleotide) encoding the motif was short, having just 15 nucleotides, and had a high g/c content. Additionally, similar sequences are contained within cDNA encoding proteins other than hemopoietin receptors, starting with various collagens that are thought to be widely distributed and also have high expression amounts, which makes the screening by the above-mentioned plaque hybridization and RT-PCR extremely inefficient.

Paragraph beginning at page 4, line 15, has been amended as follows:

The above nucleotide sequence was used to design specific oligonucleotide primers. The primers were used to perform 5'- and 3'-RACE using cDNA libraries from human fetal hepatocytes and human placenta as the template. As a result, a full-length cDNA, NR10.1, encoding a transmembrane receptor of 652 amino acids was isolated, and the whole nucleotide sequence was determined. At the same time, a cDNA clone, NR10.2, presumed to be a splice variant of NR10, was also successfully isolated from the 3'-RACE product. Based on the determined nucleotide sequence, NR10.2 was suggested to encode a soluble receptor-like protein of 252 amino acids. It was revealed that the cysteine residues, proline-rich motif, and WSXWS (SEQ ID NO:22) motif, in the extracellular domain that is conserved among the receptor family members, the box1 motif in the intracellular domain that is implicated in signal transduction, and so on were well conserved in the primary structure of NR10.1. Therefore, NR10.1 was considered to encode a typical hemopoietin receptor.

Paragraph beginning at page 36, line 9, has been amended as follows:

FIG. 1 [is a]shows the nucleotide sequence of AQ022781 (SEQ ID NO:34) identified in the gss database. The deduced amino acid sequence (SEQ ID NO:35) is shown under the predicted exon sequence. The YR motif and WS motif that were used as the target are boxed. Two "n" in the nucleotide sequence are also boxed.

Paragraph beginning at page 36, line 13, has been amended as follows:

FIG. 2 shows partial amino acid sequences of NR10 (amino acid residues 198-238, 201-237, 196-237, 189-238, and 196-239 of SEQ ID NO:4, respectively) found in the sequence of AQ022781 (SEQ ID NO:35, which is part of SEQ ID NO:4), and those of known hemopoietin receptors having homology thereto. Identical residues are boxed with shadow, and similar residues are shadowed. Gap spaces are underlined. Known hemopoietin receptors are, from top, human gp130 (GenBank Accession No. NM002184.1; IL6ST; SEQ ID NO:36), human LIF receptor (GenBank Accession No. NM002310.1; LIFR; SEQ ID NO:37), human Oncostatin M receptor  $\beta$  subunit (GenBank Accession No. NM003999.1; OSMR; SEQ ID NO:38), human IL-

12 receptor  $\beta$ 2 subunit (GenBank Accession No. NM001559.1; IL12RB2; SEQ ID NO:39), and human NR6 (GenBank Accession No. AC003112; SEQ ID NO:40).

Paragraph beginning at page 36, line 21, has been amended as follows:

FIG. 3 shows the nucleotide sequence of the full length NR10.1 cDNA (SEQ ID NO:1) that was obtained by combining the 5'- and 3'-RACE products. The deduced amino acid sequence [encoding]encoded by NR10.1 is also shown (SEQ ID NO:2). The amino acid sequence predicted to be the secretion signal sequence is underlined. The predicted transmembrane domain is shadowed. Conserved cysteine residues and the WS motif are boxed.

Paragraph beginning at page 36, line 28, has been amended as follows:

FIG. 6 shows the nucleotide sequence of the full length NR10.2 cDNA (SEQ ID NO:3) that was obtained by combining the 5'- and 3'-RACE products. The deduced amino acid sequence [encoding]encoded by NR10.2 is also shown (SEQ ID NO:4). The predicted secretion signal sequence is underlined. Conserved cysteine residues and the WS motif are boxed.

Paragraph beginning at page 37, line 14, has been amended as follows:

FIG. 13 shows the nucleotide sequence of the full length NR10.3 cDNA (SEQ ID NO:16). The deduced amino acid sequence [encoding]encoded by NR 10.3 is also shown (SEQ ID NO:17). The predicted secretion signal sequence is underlined. The amino acid sequence predicted to be the transmembrane domain is colored. Conserved cysteine residues and the WS motif are boxed.

Paragraph beginning at page 37, line 25, has been amended as follows:

The inventors aimed at finding another motif conserved among the hemopoietin receptor family, in addition to the Trp-Ser-Xaa-Trp-Ser (SEQ ID NO:22) motif (WS motif), in order to design an oligonucleotide probe including both motifs together. The inventors examined the sequence of other regions for another motif. As a result, they found a tyrosine or histidine residue in the extracellular domain of the family proteins, located 13 to 27 amino acids upstream